MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE
DEPARTMENT OF PEDIATRICS

Lecture № 13

CHRONIC LUNG INFLAMMATION. CYSTIC FIBROSIS

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LUNG INFLAMMATION

- **Acute lung inflammation** (acute pneumonia) – duration up to 3 weeks
- **Protracted pneumonia** – 6-8 weeks
- **Recurrent pneumonia** – 3 and more times at the same place
- **Chronic pneumonia** – duration more than 3 months

CHRONIC PNEUMONIA

- **Chronic** lung inflammation with **non –reversible** morphologic parenchymal changes in a **particular** lung segment or lobe - **fibrosis** and **pneumosclerosis** with **intermittent exacerbation and remission**
- Exclusion of all diffuse and extending lung diseases in systemic or congenital disorders like : hemosiderosis, mucoviscidosis, etc, and also exclusion of the specific lung inflammation, typical for tuberculosis
- Some data show equivalence between chronic pneumonia and bronchiectasis

CHRONIC PNEUMONIA (CP)

- Incidence of CP – 1-3% of children with pulmonary diseases, more often in school age
- Etiology of CP : secondary disease after a protracted or acute pneumonia : acute pneumonia in neonatal or early infant period, BPD, foreign body aspiration, congenital lung abnormalities, immune deficiency disorders, GER, rickets, hypotrophia, after measles and pertussis
- Microbiology characteristics of CP : mixed microbial flora
- Pathogenesis of CP: impaired bronchial drainage ➹ purulent endobronchitis➹lung destruction ➹ bronchiectasis ➹ chronic lung failure and cor pulmonale

CHRONIC PNEUMONIA

Clinical characteristics:

- ✓Cough- persistent, in the mornings, wet, with a lot of muco-purulent flam
- ✓Change of external appearance- paleness, failure to thrive
- ✓Chronic hypoxia: changes of the nails, cor pulmonale
- ✓Auscultation: bronchitis: wheezing or wet crackles, localized
- ✓"Middle lobe" syndrome

CHRONIC PNEUMONIA

- X-ray :"Honeycomb" image: atelectasis, emphysema, fibrosis
- Bronchoscopy, bronchography
- Lab parameters, microbiology
- PFT test – restrictive pulmonary failure

Evolution : chronic course : **remission and exacerbation**

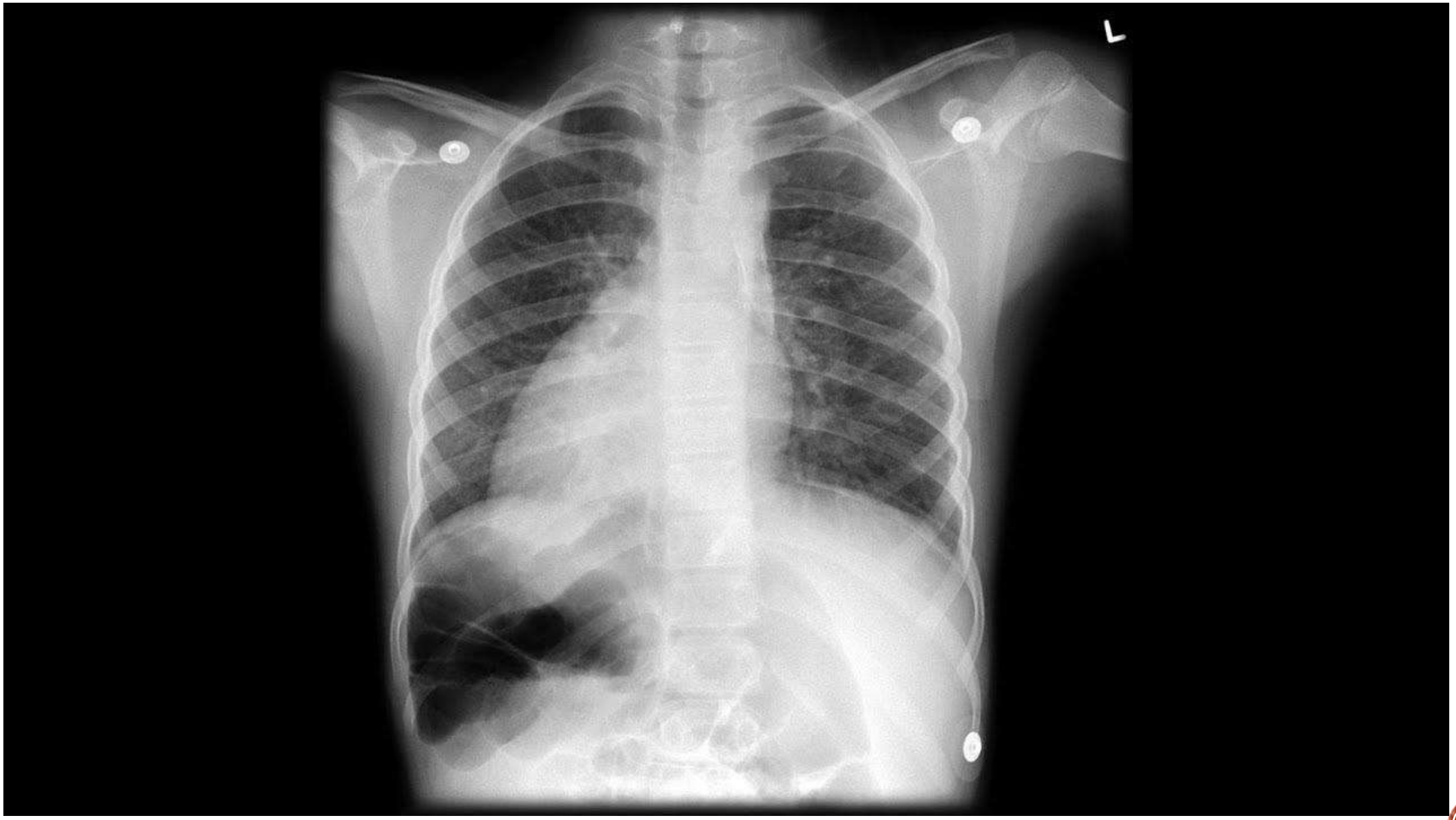
DD: TBC, CF, protracted pneumonia, interstitial fibrosis, etc.

Treatment : - mucolytics, antibiotics, inhalations, physiotherapy

- lung operation in case of local bronchiectasis

KARTAGENER SYNDROME

- Triade : **situs viscerus inversus+bronchiectasis+pansinuitis**
- ARD genetic disease, incidence : 1:1 500 -1:30 000
- Pathophysiology: ciliar dyskinesia due to a loss of dynein protein in cilia➐impaired muco-ciliar transport
- Cilia defect affects **middle ear** , **sinuses** and **bronchi**, also **spermatozoids**
- Clinical symptoms : chest deformities, cough (wet and deep), heart pick in the right chest part, failure to thrive, nasal polyps, purulent nasal secretions, dyspnea, etc.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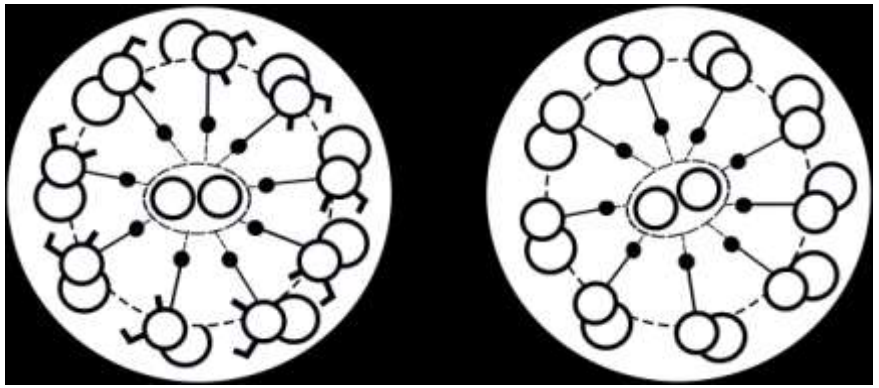
KARTAGENER SYNDROME

- X – ray: inverted organs, diffuse changes into lung bases
- PFT – restrictive and obstructive lung changes
- Low levels of IgA
- FBS, MRI
- DD: dextrocardia, s-me Chandra – Khetarpal, s-me Turpin, etc.
- Treatment : complex treatment : bronchial drainage, mucolitics, antibiotics, etc.

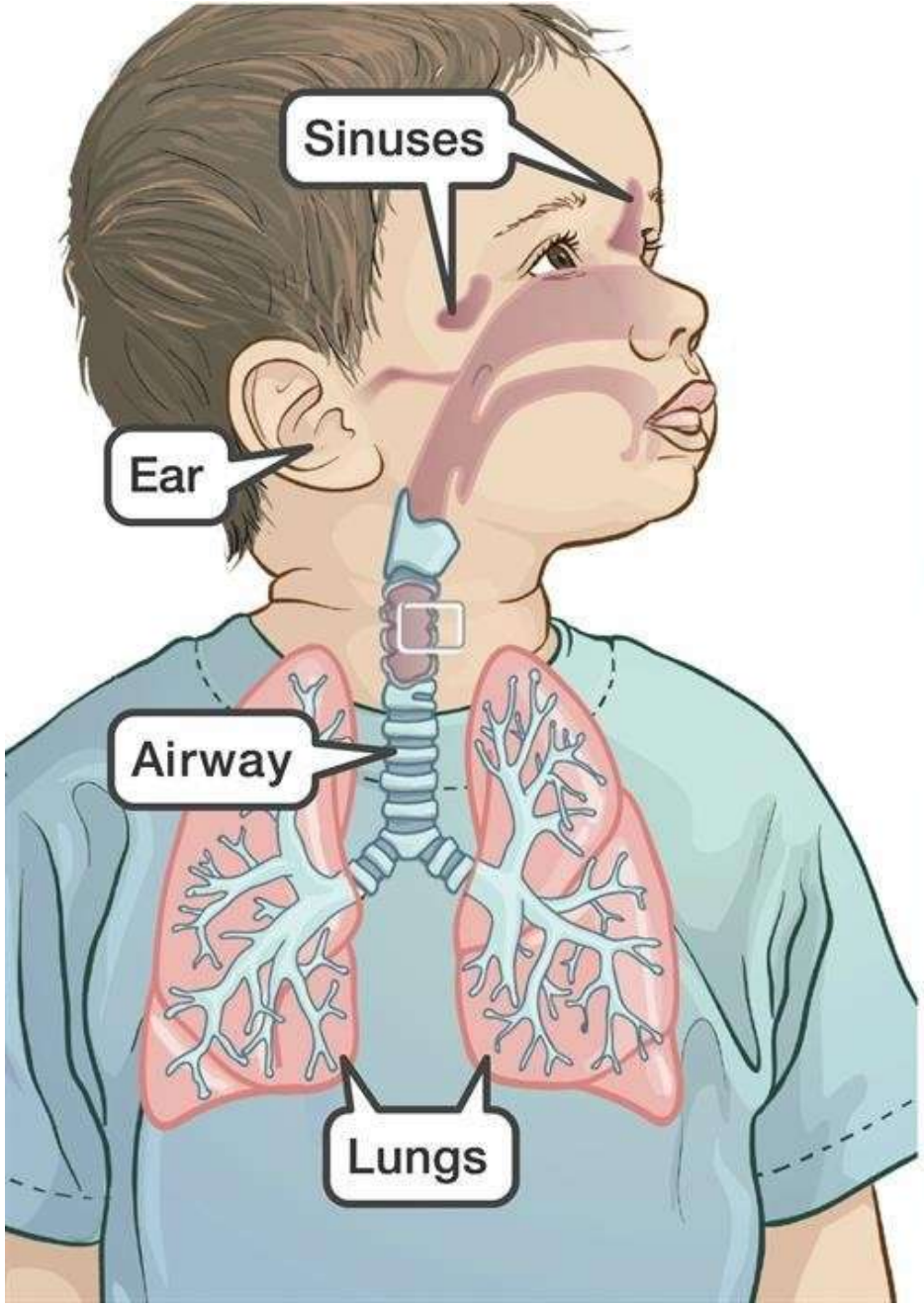
PRIMARY CILIARY DYSKINESIA (PCD)

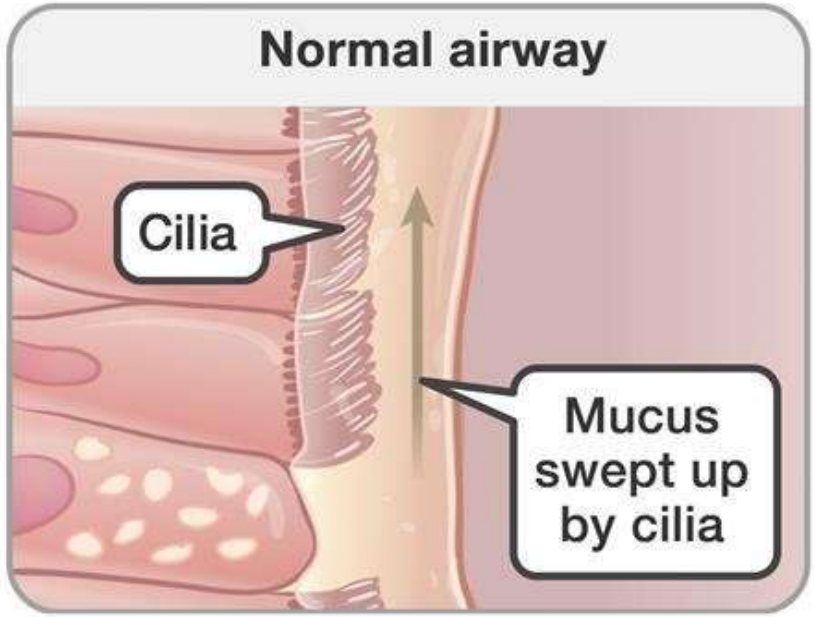
- Abnormal ciliar function and structure, impaired bronchial drainage, recurrent sino – pulmonal disease
- Incidence: 1:40000
- ARD disorder, defect of dineyn synthesis
- PCD is associated with situs inversus, liver and kidney cysts, biliary atresia and bronchiectasis

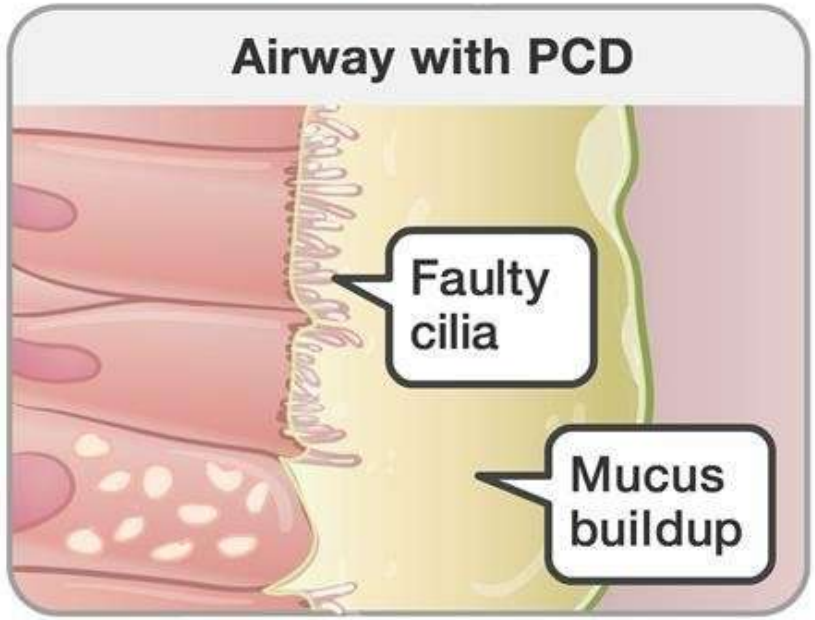


PCD

- Infection of lower respiratory tract , chronic cough, muco-purulent secretions, wheezing, dyspnea
- Chronic rhinitis, sinusitis, middle ear infection
- Diagnostic tests: screening tests: nasal NO, saccharin test , electron microscopy
- Colonization : H. influenzae, Ps. Aeruginosa, S.aureus, S. pneumoniae
- Treatment : aggressive treatment of exacerbations : antibiotics (oral + inhaled), mucolytics, inhalations







EOSINOPHILIC PNEUMONIA (EP)

- Eo infiltration in the lung interstitium and alveoli
- EP can be primary (idiopathic) or secondary (due to specific medications of ABPA, tumors, etc.)
- EP can be acute or chronic in course
- Loffler syndrome is a rare case of EP, pulmonary failure, Eo migrating infiltrates , blood Eo
- Idiopathic acute and chronic EP : cough, fatigue, chest pain, arthralgias, myalgias, blood Eo, atopy, BLA with Eo infiltration
- Churg – Strauss syndrome : vasculitis of the small and medium vessels with **Triade : asthma, allergic rhinitis, hyper Eo**

CHURG-STRAUSS SYNDROME

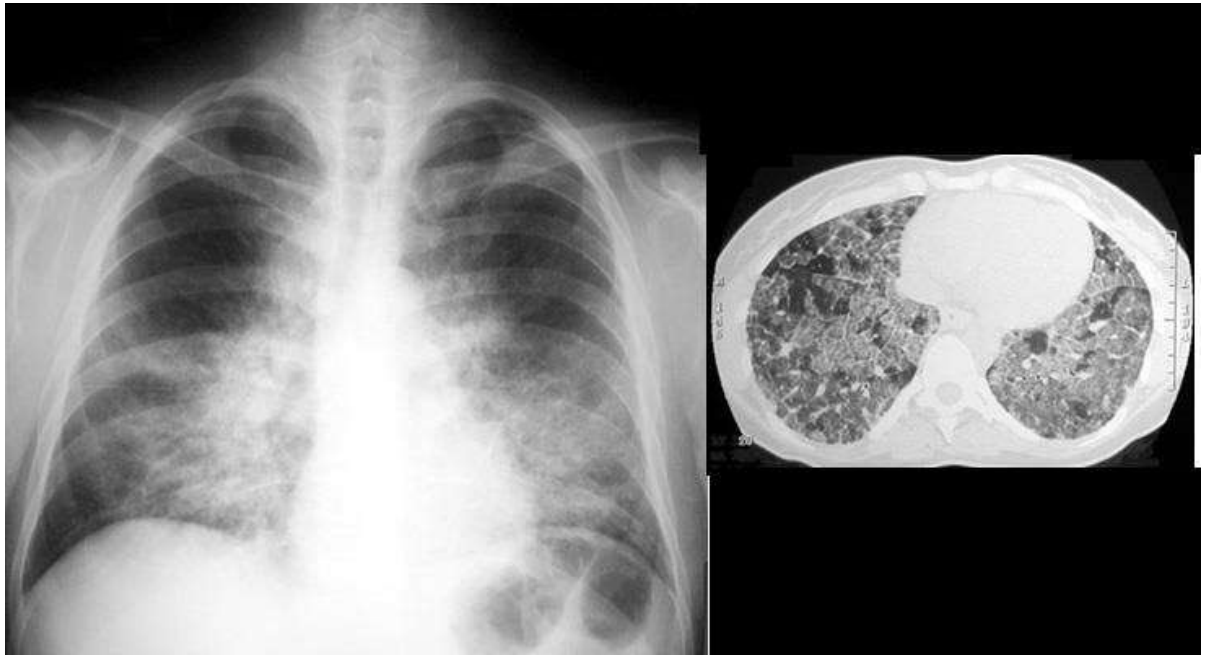
3 Clinical phases

Prodromal Phase	Eosinophilic phase	Vasculitic phase
• Late onset allergic rhinitis and atopy* • Lasting for >10 years	• Marked blood eosinophilia • Eosinophillic infiltration of lung, GI tract or skin	• Vasculitis of the small and medium vessels • Vascular and extravascular granulomas • Constitutional symptoms • Worsening asthma symptoms

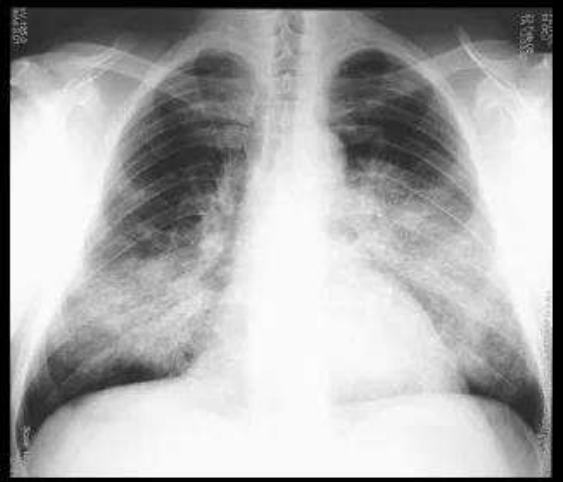
PULMONARY ALVEOLAR PROTEINOSIS (PAP)

- Described by Rosen in 1958 – Castleman- microscopic changes into the alveoli, PAS positive
- PAP could be **congenital** or **acquired**
- Congenital PAP : neonatal RDS, autosomal recessive disorder(ARD), disturbance of surfactant metabolism : SP- B, SP – C. This form can be diagnosed by a gene diagnosis, BAL analysis, high LDH level
- Acquired PAP: non – productive cough, dyspnea, cyanosis, chest pain, hemoptoe, failure to thrive, reduced weight
- Treatment of PAP : bronchial lavage, gene therapy, lung transplantation

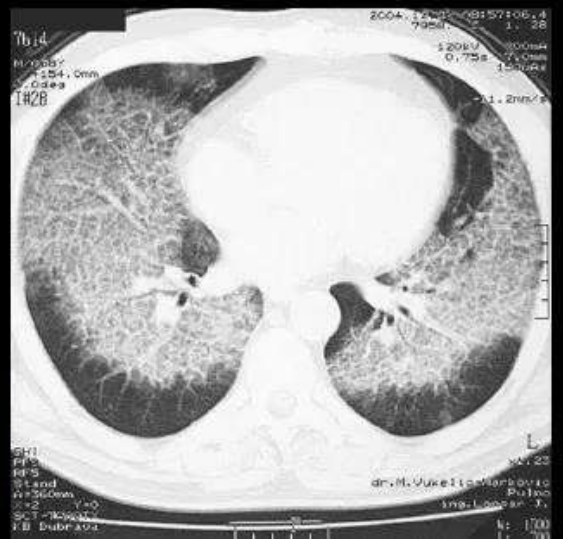
PAP



Pulmonary Alveolar Proteinosis



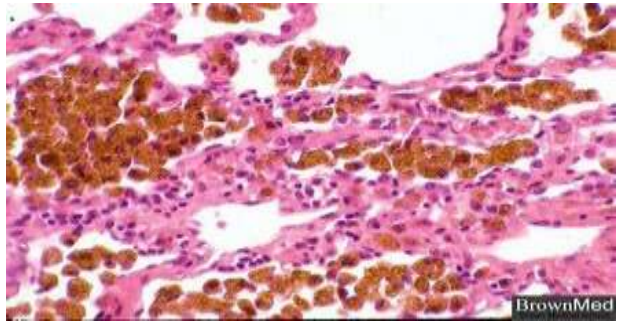
thickened interlobular septa
"crazy paving" ground glass fashion, sharply demarked from normal lung creating a "geographic" pattern.



diffuse reticulo-alveolar infiltrates
BAT WING distribution

BAL:- milky effulent foamy macrophages with lipoproteinous intraalveolar material

PULMONARY HEMOSIDEROSIS



- Primary disease, hypersensitivity to a cow milk (immune response), or combination with nephritis (Goodpasture syndrome)
- Clinical findings: **attacks of pulmonary interstitial hemorrhages** + **hypochromic microcytic anemia with low serum iron**
- Contract of minimal physical findings with severe general condition and deterioration, followed by respiratory failure
- In severe crisis a hemorrhage shock could be observed, also jaundice and HSM
- Pulmonary X – ray: perihilar infiltrates, atelectasis, adenopathy, emphysema, PFT – restriction
- Diagnosis : hemosiderophages in sputum and BAL, typical clinical and lab
- Treatment : oxygen, hemotrasfusions, CS, Desferal, poor prognosis

IDIOPATHIC PULMONARY FIBROSIS

- Also called Hamman Rich syndrome
- Unclear etiology, rare in childhood
- Clinical symptoms : dyspnea, cough, tachypnea, cyanosis, chronic cor pulmonale
- Physical examination is insufficient , X – ray : interstitial infiltrates mainly in the lung bases
- No specific treatment, poor prognosis

In the group of chronic lung diseases also must be pointed : pulmonary alveolar microlithiasis and alfa 1- AT deficiency

CYSTIC FIBROSIS

- **Incidence** : cystic fibrosis (CF) is the most frequent lethal genetic disorder in white people, 1: 3000 for white race, 1:10 000 hispano – Americans, 1:20 000 African people
- ARD , 7q- chromosome ❼ CFTR , over 1600 mutations, more than 50% delta F508, six classes of CFTR mutations
- No correlation between genotype and phenotype, genotype is connected only with pancreatic sufficiency
- CFTR gene is cloned in 1989, also important the role of modifying genes

CYSTIC FIBROSIS

- **Pathophysiology**: **"low volume"** hypothesis : reabsorption of sodium, decreased secretion of chloride ➡ passive H_2O movement ➡ surface dehydration ➡ impaired microcellular clearance ➡ bacterial invasion (S.aureus, H influenzae, Ps. Aeruginosa)
- Vicious circle : **infection ➡ inflammation ➡ tissue damage**
- Affected organs : skin, exocrine pancreas, gastro-intestinal tract, reproductive system, respiratorysystem
- Secondary involved : endocrine pancreas, muscle and bones, CNS, kidneys , etc.

DIAGNOSIS OF CF

- Middle age of diagnosis : 6 months
- Clinical symptoms : respiratory symptoms 50%, malnutrition and failure to thrive 34%, diarrhea 26%, meconium ileus 21%, family history 16%, metabolic alkalosis
- Neonatal screening (since 2008) – IRT
- Sweat test : positive above 60 mmol/l, negative below 30(40), borderline : 30-60 mmol/l
- Sweat test could be false positive or false negative!!!
- Fecal elastase <100 mcg
- Steatorrhea
- Genetic test ,NPD

CF – CLINICAL SYMPTOMS – MULTIORGAN DISEASES

- A. **Respiratory system :**

✓URA: chronic sinusitis, nasal polyposis

✓LRA: chronic pneumonia, bronchiectasis, wheezing

✓Complications : atelectasis, pneumothorax, hemoptysis, ABPA, respiratory failure, cor pulmonale

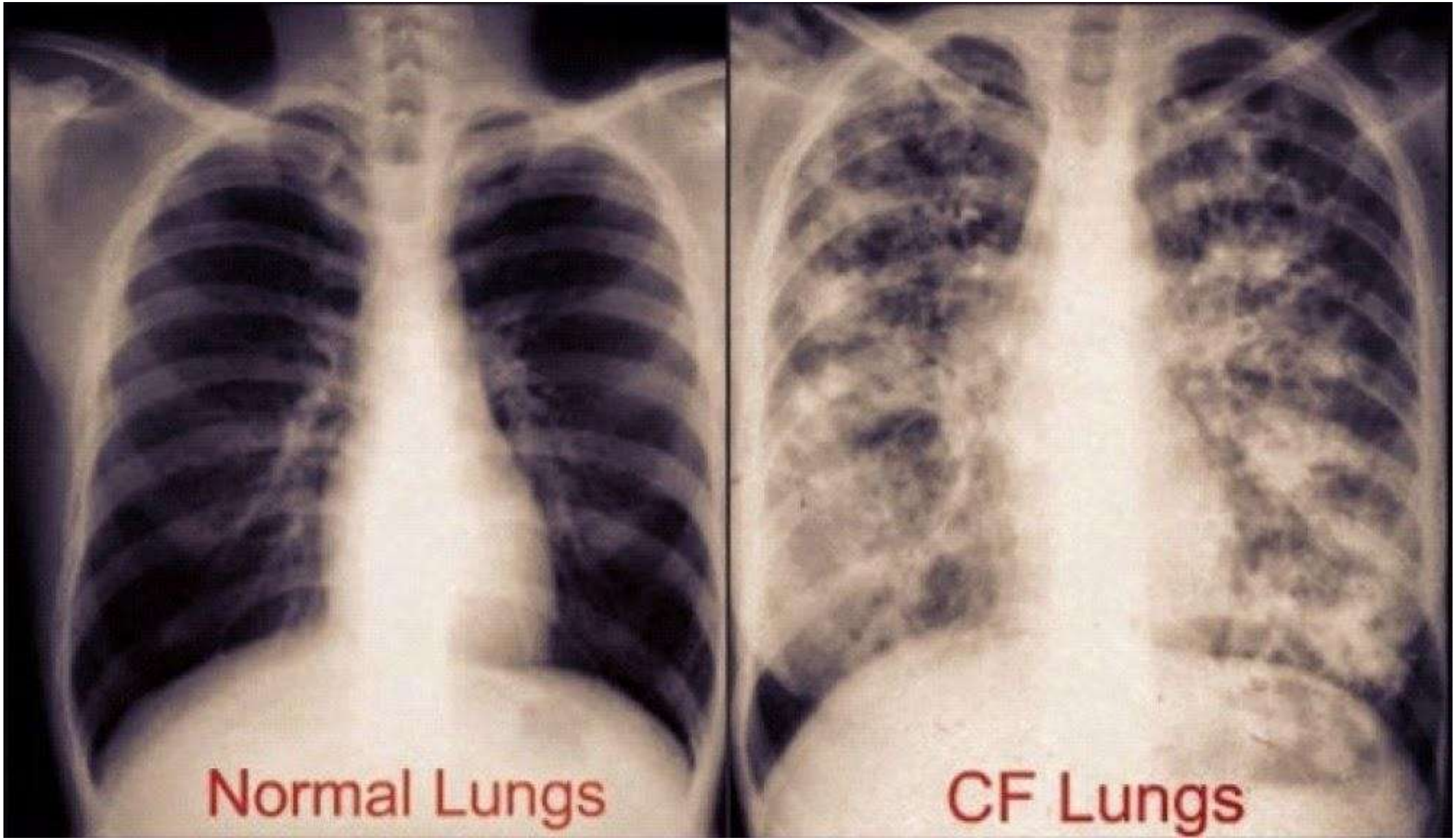
✓Typical bacterial agents: S.aureus, H.influenzae, Ps. Aeriginosa, Stenotrophomonas maltophilia, Burkhordelia sepacia, non TBC mycobacteria, Aspergillus fumigatus

CF – PULMONARY COMPLICATIONS

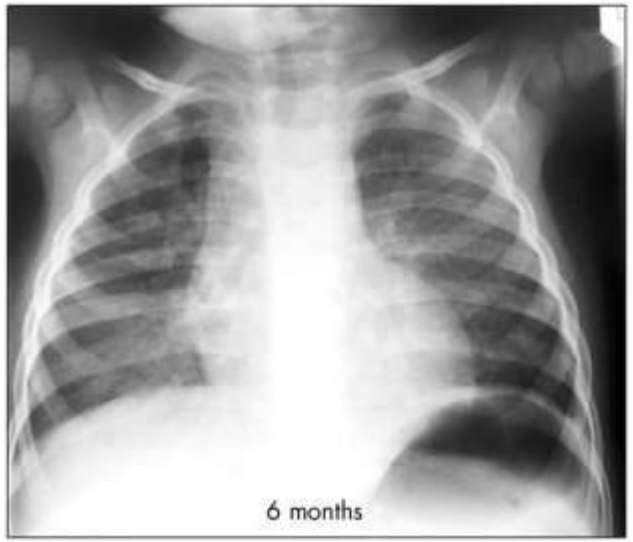
- In FEV1<30%, PaO2<55 mm, PaCO2>50 mm – end – stage of the disease – lung transplantation
- Clinical symptoms up to the age of 1 year :

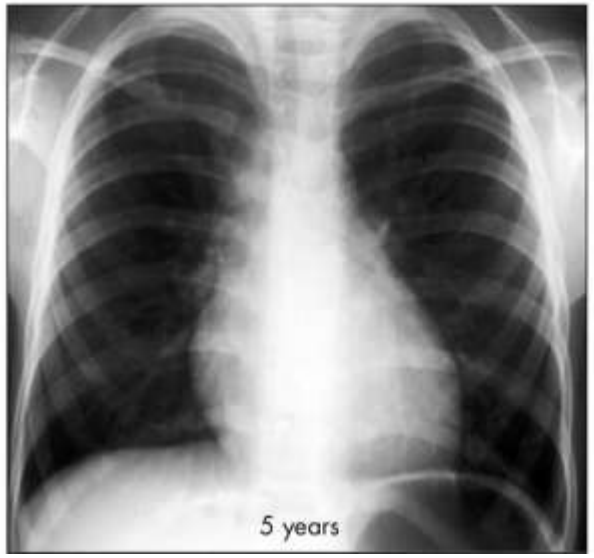
wheezing bronchitis with difficult treatment,

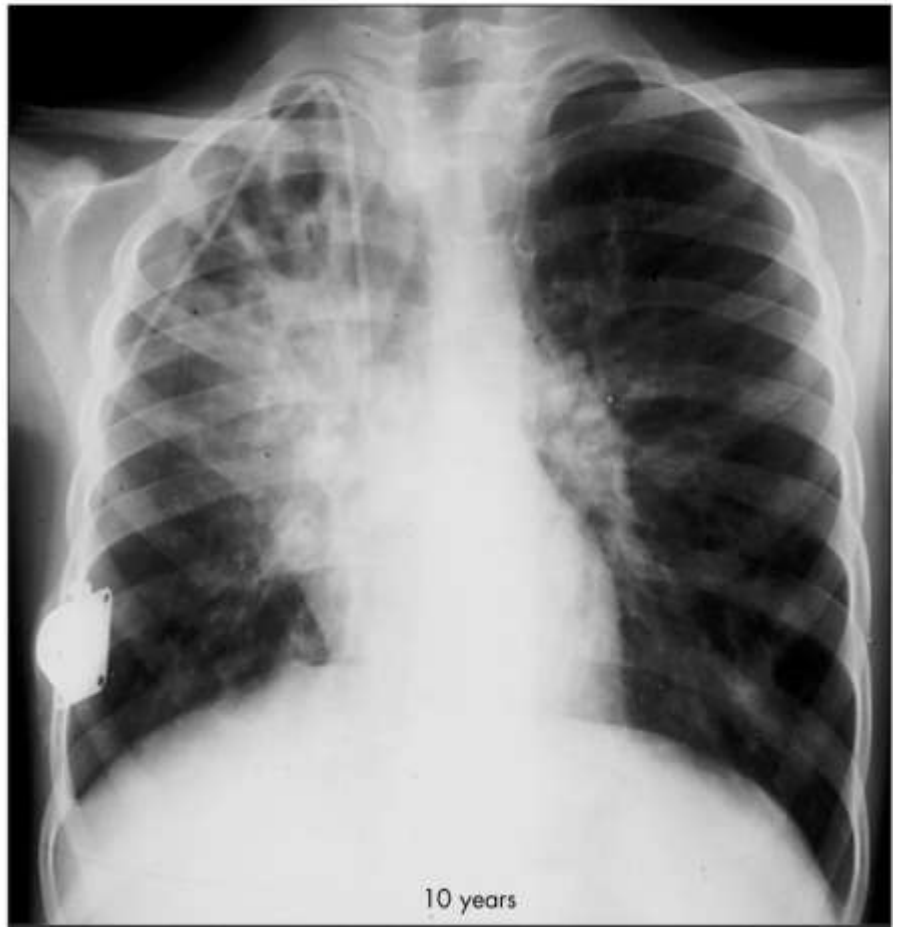
than – recurrent pneumonias, after 3 yeas of life : bronchiectasis


Normal Lungs
CF Lungs

CF LUNGS







CF – CLINICAL MANIFESTATIONS

B. **GI manifestation**

- ✓Meconium ileus at birth- 15%
- ✓Rectal prolapse
- ✓More than 90% - pancreas insufficiency : steatorrhea, flatulence, failure to thrive, diarrhea, malnutrition and vit.deficinecy
- ✓Distal obstructive syndrome (DIOS)
- ✓Low vit A, D, E, K – anemia, neuropathy, osteoporosis, bleeding, poor night sight, etc.
- ✓GERD
- ✓Pancreatitis, biliary cirrhosis

CF – CLINICAL MANIFESTATIONS

C. **Electrolyte disturbances**

✓Hypo K+

✓Hypo Na+

✓Metabolic alkalosis

✓Hypotonic dehydration

D. **Reproductive problems:**

✓Azoospermia, congenital occlusion of vas deference

✓Thick cervical mucous in females

CF- CLINICAL MANIFESTATIONS

E. **Other symptoms:**

✓Impaired glucose tolerance, diabetes mellitus :

annually blood sugar and oral glucose tolerance test.

Diabetes is with low insulin secretion , ketoacidosis is quite rare.

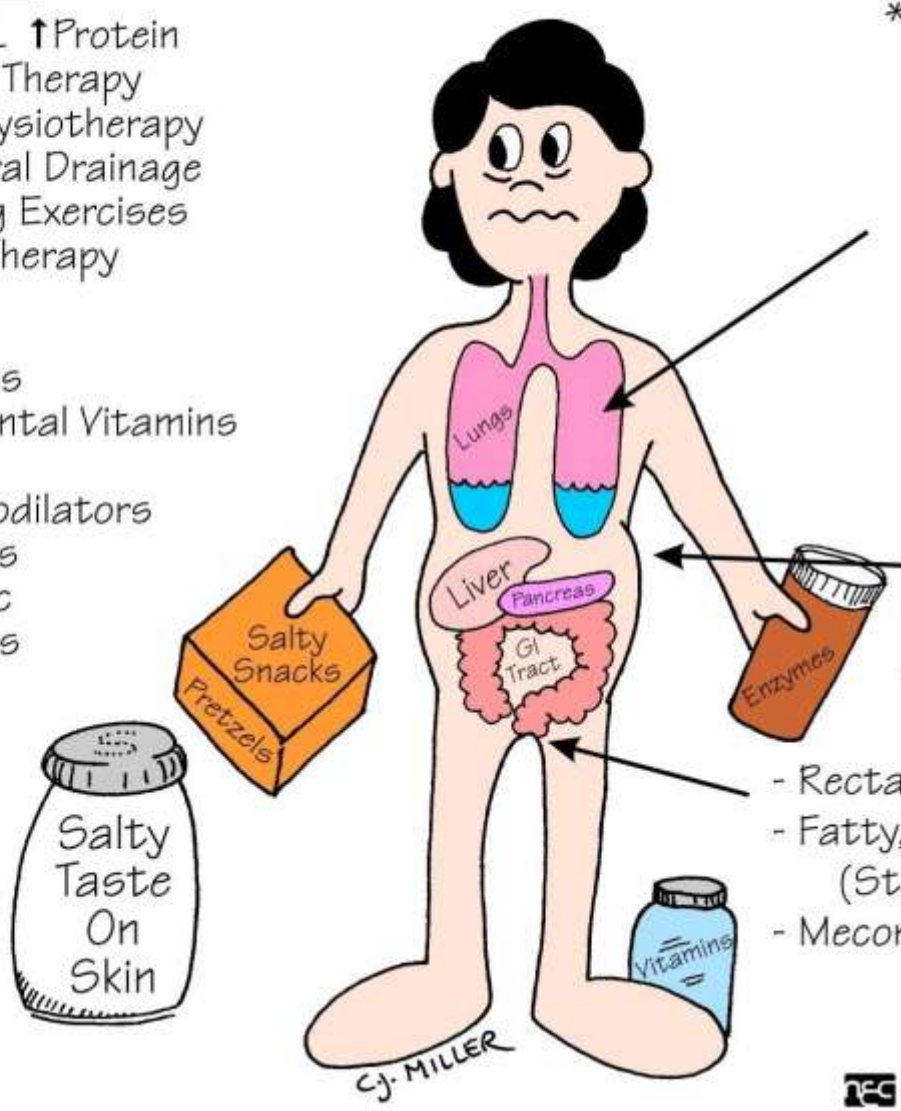
No immune mechanism, no antibodies.

✓Osteoporosis due to low vit D, chronic inflammation, steroid usage

CYSTIC FIBROSIS (CF)

* Treatment *

- Diet: ↑CAL ↑Protein
- Pulmonary Therapy
  - Chest Physiotherapy
    - Postural Drainage
  - Breathing Exercises
  - Aerosol Therapy
- Meds
  - Antibiotics
  - Supplemental Vitamins
  - Aerosol Bronchodilators
  - Mucolytics
  - Pancreatic Enzymes



* Symptoms *

- Fatigue
- Chronic Cough
- Recurrent URI's
- Thick, Sticky Mucus
- Chronic Hypoxia: Clubbing, Barrel Chest
- ↓ Absorption of Vitamins and Enzymes
- Abdominal Distention
- ↓ Digestive Enzymes
- Rectal Prolapse
- Fatty, Stinky Stools (Steatorrhea)
- Meconium Ileus in Newborn

CF – TREATMENT : CF CENTERS

1. **Pancreatic enzyme replacement therapy:**

- 500 – 2000 U/kg lipase per meal
- Fat dissolved vitamins
- Ursofalk 20 mg/kg/day
- Increase salt intake
- Monitoring of BW, BH, BMI

CF TREATMENT

2. **Pulmonary treatment**

a/ **Bronchial obstruction**

- Clearance of bronchial tree, drainage, PEP mask, Vest – method, “Flutter”
- Bronchodilators : in 25% of CF patients are used without stopping, or in need
- Pulmozyme (Dornase alfa) – after 5 year of age, improves mucocilliar transport
- Hypertonic (3-6-7%) saline water solution

CF TREATMENT

b/**Pulmonary infections**

- AB courses with high doses and duration 14-21 days
- Inhalatory options : Colistin, Tobramycin, Amikacin
- Oral courses
- Intravenous courses : anti – Pseudomonas groups
- Mucolytics

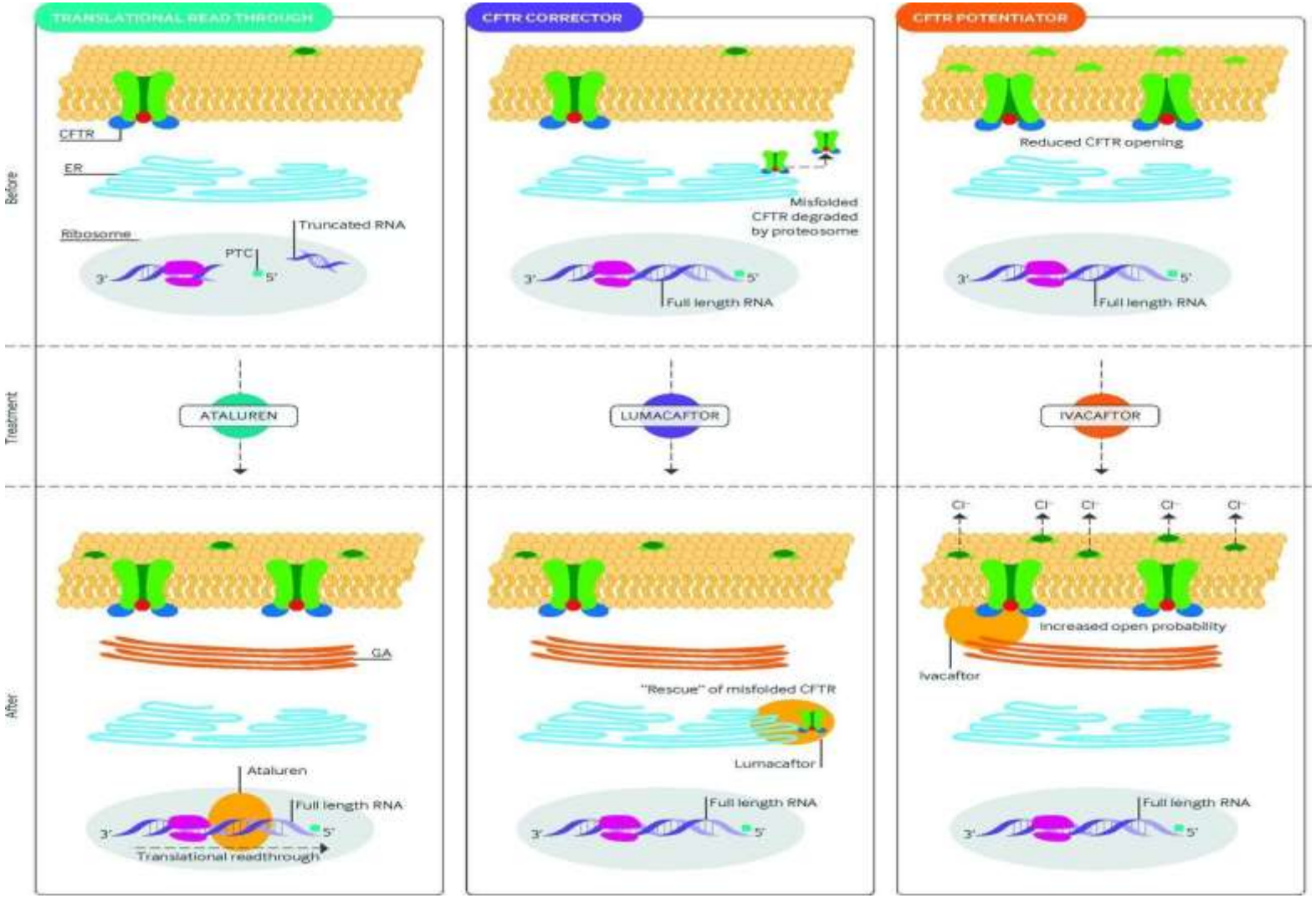
c/ **Anti- inflammatory medications**

- Corticosteroids : Systemic and inhaled
- Ibuprofen
- Macrolydes

CF FOLLOW UP

- Physical examination : every 3 months
- Spirometry : 2-4 times per year
- Microbiology specimen – every 3 months
- Lab parameters – every 6 months
- X – ray – in need, CT scan, MRI
- New biological treatment – target therapy

TARGET THERAPY OF CF



Thank you for your attention !